

SPECIFICATION AMENDMENTS

Please amend the ABSTRACT as follows:

ABSTRACT

B¹ The present invention provides chimeric ~~GPCRs that display novel downstream signaling properties~~ Edg receptors, useful as components of an assay system. The present invention also provide methods of screening for compounds that bind a chimeric Edg receptor, for example, by contacting a chimeric Edg receptor with a compound and detecting a change in chimeric Edg receptor-mediated activity such as calcium mobilization.

SPECIFICATION AMENDMENTS

Please amend the specification as follows:

Amend the paragraph beginning on page 7, line 18, as indicated by the underlined portion, and amend the subsequent table by adding the words "Table 1" and enlarging the font size of the lettering used in the table, as shown below:

The amino acid notations used herein for the twenty genetically encoded L-amino acids are conventional and are as shown in Table 1. follows:

Table 1

Amino Acid	One-Letter Abbreviation	Three Letter Abbreviation
Alanine	A	Ala
Arginine	R	Arg
Asparagine	N	Asn
Aspartic acid	D	Asp
Cysteine	C	Cys
Glutamine	Q	Gln
Glutamic acid	E	Glu
Glycine	G	Gly
Histidine	H	His
Isoleucine	I	Ile
Leucine	L	Leu
Lysine	K	Lys
Methionine	M	Met
Phenylalanine	F	Phe
Proline	P	Pro
Serine	S	Ser
Threonine	T	Thr
Tryptophan	W	Trp
Tyrosine	Y	Tyr
Valine	V	Val

Amend Table 2, beginning on page 18, line 13, by changing the font size and spacing as indicated below (no additions or deletions are to be made to Table 2):

Table 2

Amino Acid Sequences of Edg Receptors

Human Edg 1 (SEQ ID NO: 1)	MGPTSVPLVKAHRSSVSDYVNYDIIVRHYNITGKLNISAD KENSIKLTSVVFILICCFIILENIFVLLTIWKTKKFHRPM YYFIGNLALSDDLAVAYTANLLLSGATTYKLTTPAQWFLR EGSMFVALSASVFSLLAIAIERYITMLKMKLHNGSNNFRL FLLISACWVISLILGGLPIMGWNCISALSSCSTVLPPLYHK HYILFCTTVFTLLLLSIVILYCRIYSLVRTRSRRLTFRKN ISKASRSSEKSLALLKTVIIVLSVFIACWAPLFIILLLDV GCKVKTCDILFRAEYFLVLAVLNSGTNP IIYTLTNKEMRR AFIRIMSCCKCPSGDSAGKFKRPIIAGMEFSRSKSDNSSH PQKDEGDNPETIMSSGNVNSSS
Genbank Accession No. AF233365	
Human Edg2 (SEQ ID NO:30)	MAAISTSI PVISQPQFTAMNEPQCFYNESIAFFYNRSGKH LATEWNTVSKLVMGLGITVCI FIMLANLLVMVAI YVNRRF HFPIYYLMANLAAADFFAGLAYFYLMFNTGPNTRRLTVST WLLRQGLIDTSLTASVANLLAIAIERHITVFRMQLHTRMS NRRVVVVIVVIWTMAIVMGAIPSVGWNCICDIENCSNMAP LYSDSYLVFWAIFNLVTFVVMVLYAHIFGYVRQRTMRMS RHSSGPRRNRDTMMSLLKTVVIVLGAFIICWTPGLVLLLL DVCCPQCDVLAYEKFFLLLAEFNSAMNP IIYSYRDKEMSA TFRQILCCQRSENPTGPTGSDRSASSLNHTILAGVHSND HSVV
Genbank Accession No. U78192	
Human Edg 3 (SEQ ID NO:2)	MATALPPRLQPVRGNETLREHYQYVGKLAGRLKEASEGST LTTVLFLVICSFIVLENLMVLIAIWKNNKFHNRMYFFIGN LALCDLLAGIAYKVNILMSGKKTFSLSPTVWFLREGSMFV ALGASTCSLLAIAIERHLTMIKMRPYDANKRHRVFLLLIGM CWLIAFTLGALPILGWNC LHNLPDCSTILPLYSKKYIAFC ISIFTAILVTIVILYARIYFLVKSSSRKVANHNNSERSMA LLRTVVIVVSVFIACWSPLFILFLIDVACRVQACPILFKA QWFIVLAVLNSAMNPVIYTLASKEMRRRAFFRLVCNCLVRG RGARASPIQPALDPSRSKSSSSNNSSHSPKVKEDLPHTDP SSCIMDKNAALQNGIFCN
Genbank Accession No. X83864	

Human Edg4
(SEQ ID NO:31)

Genbank
Accession No.
AF233092

MVIMGQCYNETIGFFYNNSGKELSSHWRPKDVVVVALGL
TVSVLVLLTNLLVIAAIA SNRRFHQPIYYLLGNLAAADLF
AGVAYLFLMFHTGPRTARLSLEGWFLRQGLDTSLTASVA
TLLAIAVERHRSVMAVQLHSRLPRGRVVMLIVGVWVAALG
LGLLPAHSWHCLCALDRCSRMAPLLSRSYLAVWALSLLV
FLLMVAVYTRIFFYVRRRVQMAEHVSCHPRYRETTLSLV
KTVVILGAFVVCWTPGQVVLLLDGLGCESC NVLAVEKYF
LLLAEANS LVNAAVYSCRDAEMRRTFRRLLCCACLRQSTR
ESVHYTSSAQGGASTRIMLPENGHPLMDSTL

Human Edg 4 mt
(SEQ ID NO:32)

Genbank
Accession No.
AF011466

MVIMGQCYNETIGFFYNNSGKELSSHWRPKDVVVVALGL
TVSVLVLLTNLLVIAAIA SNRRFHQPIYYLLGNLAAADLF
AGVAYLFLMFHTGPRTARLSLEGWFLRQGLDTSLTASVA
TLLAIAVERHRSVMAVQLHSRLPRGRVVMLIVGVWVAALG
LGLLPAHSWHCLCALDRCSRMAPLLSRSYLAVWALSLLV
FLLMVAVYTRIFFYVRRRVQMAEHVSCHPRYRETTLSLV
KTVVILGAFVVCWTPGQVVLLLDGLGCESC NVLAVEKYF
LLLAEANS LVNAAVYSCRDAEMRRTFRRLLCCACLRQSTR
ESVHYTSSAQGGASTRIMLPENGHPLMTPPF SYLELQRYA
ASNKSTAPDDLWVLLAQPNQQD

Human Edg 5
(SEQ ID NO:33)

Genbank
Accession No.
AF034780

MGSLYSEYLNPNKVQEHYNYTKETLETQETTSRQVASAFI
VILCCAIVVENLLVLI AVARN SKFHSAMYLFLGNLAASDL
LAGVAFVANTLLSGSVTLRLTPVQWFAREGSASITLSASV
FSL LAIAI ERHVAIAKV KLYGSDKSCRMLLLIGASWLI SL
VLGGLPILGWNCLGHLEACSTVLPYAKHYVLCVVTIFSI
ILLAI VALYVRIYCVVRSSHADMAAPQTLALLKTVTIVLG
VFIVCWLP AF SILLDYACPVHSCPILYKAHYFFAVSTLN
SLLNPVIYTWRSRDLRREVL RPLQCWRPGVG VQGRRRVGT
PGHLLPLRSSSSLERGMHPTSPTFLEGNTVV

Human Edg6
(SEQ ID NO:34)

Genbank
Accession No.
AJ000479

MNATGTPVAPESCQQLAAGGHSRLIVLHYNHSGRLAGRGG
PEDGGLGALRGLSVAASCLVLENLLVLAAI TSHMRSRRW
VYYCLVNITLSDLLTGAAYLANVLLSGARTFRLAPAQWFL
REGLLFTALAASTFSL LFTAGERFATMVRPVAESGATKTS
RVYGFIGLCWLLAALLGMLPLLGNCLCAFDRCSSLLPLY
SKRYILFCLVIFAGVLATIMGLYGAI FRLVQASGQKAPRP
AARRKARRLLKTVLMILLAFLVCWGPLFGLLLADVFGSNL
WAQEYLRGMDWILALAVLNSAVNP I IYSFRSREVCRAVLS
FLCCGCLRLGMRGPGDCLARAVEAHSGASTTDSSLRPRDS
FRGSRSL SFRMREPLSSISSVRSI

Human Edg7
(SEQ ID NO:35)

Genbank
Accession No.
AF127138

MNECHYDKHMDFFYNRSNTDTVDDWTGTKLVIVLCVGTFF
CLFIFFSNSLVIAAVIKNRKFHFPFYLLANLAAADFFAG
IAYVFLMFNTGPVSKTLTVNRWFLRQGLLDSSLTASLTNL
LVIAVERHMSIMRMRVHSNLTKKRVTLILLVWAIAIFMG
AVPTLGWNCLCNISACSSLAPIYSRSLVFWTVSNLMAFL
IMVVVYLRIYVYVKKRTNVLSPTHSGSISRRTPMKLMKT
VMTVLGAFVVCWTPGLVVLILLDGLNCRQCGVQHVKRWFL
LALLNSVNPPIIYSYKDEDMYGTMMKMICCFSQENPERRP
SRIPSTVLSRSDTGSQYIEDSISQGAVCNKSTS

Human Edg 8
(SEQ ID NO:36)

Genbank
Accession No.
AF317676

MESGLLRPAPVSEVIVLHYNNTGKLRGARYQPGAGLRADA
VVCLAVCAFIVLENLAVLLVLGRHPRFHAPMFLLLGSLTL
SDLLAGAAYAANILLSGPLTLKLSPALWFAREGGVFVALT
ASVLSLLAIALERSLTMARRGAPVSSRGRTLAMAAAANG
VSLLLGLLPALGWNCLGRLDACSTVLPLYAKAYVLFVLA
FVGILAAICALYARIYCQVRANARRLPARPGTAGTTSTRA
RRKPRSLALLRTL SVLLAFVACWGPLFLLLLLLDVACPAR
TCPVLLQADPFLGLAMANSLLNPPIIYTLTNRDLRHALLRL
VCCGRHSCGRDPSGSQQSASAAEASGGLRRLCLPPGLDGSF
SGSERSSPQRDGLDTSGSTGSPGAPTAARTLVSEPAAD

Amend Table 3, beginning on page 21, line 1, by changing the font size and spacing as indicated below (no additions or deletions are to be made to Table 3):

Table 3

Amino Acid Sequences of Chimeric Edg Receptors

Edg1/3(ct)
(SEQ ID NO:3)

MGPTSVPLVKAHRSSVSDYVNYDIIVRHYNNTGKLNISAD
KENSIKLTSVVFILICCFIILENIFVLLTIWKTKKFHRPM
YYFIGNLALSDDLAVAYTANLLLSGATTYKLTTPAQWFLR
EGSMFVALSASVFSLLAIAIERIYITMLKMKLHNGSNNFRL
FLLISACWVISLILGGLPIMGWNCISALSSCSTVLPLYHK
HYILFCTTVFTLLLLSIVILYCRISLVTRSRRLTFRKN
ISKASRSSEKSLALLKTVIIVLSVFIACWAPLFILLLLDV
GCKVKTCDILFRAEYFLVLAVLNSGTNPPIIYTLT**SKEMRR**
AFFRLVCNCLVRGRGARASPIQPALDPSRSKSSSSNNSSH
SPKVKEDLPHTDPSSCIMDKNAALQNGIFCN

Edg1/3(i3ct)
(SEQ ID NO:4)

MGPTSVPLVKAHRSSVSDYVNYDIIVRHYNITGKLNISAD
KENSIKLTSVVFILICCFIILENIFVLLTIWKTCKFHRPM
YYFIGNLALSDDLAVAYTANLLLSGATTYKLTTPAQWFLR
EGSMFVALSASVFSLLAIAIERYITMLKMKLHNGSNNFRL
FLLISACWVISLILGGLPIMGWNCISALSSCSTVLPLYHK
HYILFCTTVFTLLLLSIVILYCRIYSLVRSSSRKVANHNN
SERSMALLRTVIIVLSVFIACWAPLFILLLLLDVGCKVKTC
DILFRAEYFLVLAVLNSGTNP I IYTLT**SKEMRRAFFRLVC**
NCLVRGRGARASPIQPALDPSRSKSSSSNNSSHSPKVKED
LPHTDPSSCIMDKNAALQNGIFCN

Edg1/3(i2i3ct)
(SEQ ID NO:5)

MGPTSVPLVKAHRSSVSDYVNYDIIVRHYNITGKLNISAD
KENSIKLTSVVFILICCFIILENIFVLLTIWKTCKFHRPM
YYFIGNLALSDDLAVAYTANLLLSGATTYKLTTPAQWFLR
EGSMFVALSASVFSLLAIAIERH**LTMIKMRPYDANKRHRL**
FLLISACWVISLILGGLPIMGWNCISALSSCSTVLPLYHK
HYILFCTTVFTLLLLSIVILYCRIYSLVRSSSRKVANHNN
SERSMALLRTVIIVLSVFIACWAPLFILLLLLDVGCKVKTC
DILFRAEYFLVLAVLNSGTNP I IYTLT**SKEMRRAFFRLVC**
NCLVRGRGARASPIQPALDPSRSKSSSSNNSSHSPKVKED
LPHTDPSSCIMDKNAALQNGIFCN

Edg 5/3(i3ct)
(SEQ ID NO:37)

B4

MGSLYSEYLNPNKVQEHYNYTKETLETQETTSRQVASAFI
VILCCAIVVENLLVLIAVARN**SKFH**SAMYLFLGNLAASDL
LAGVAFVANTLLSGSVTLRLTPVQWFAREGSASITLSASV
FSLAIAIAIERHVAIAKV**KLYGSDK**SCRMLLLIGASWLISL
VLGGLPILGWNCLGHLEACSTVLPLYAKHYVLCVVTIFSI
ILLAIVALYVRIYCV**VKSSSRKVANHNN**SERSMALLRTVT
IVLGVFIVCWLPAFSILLLDYACPVHSCPIYKAHYFFAV
STLNSLLNPVIYTW**ASKEMRRAFFRLVCNCLVRGRGARAS**
PIQPALDPSRSKSSSSNNSSHSPKVKEDLPHTDPSSCIMD
KNAALQNGIFCN

Edg 8/4(ct)
(SEQ ID NO:38)

MESGLLRPAPVSEVIVLHYNITGKLRGARYQPGAGLRADA
VVCLAVCAFIVLENLAVLLVLGRHPRFHAPMFLLLGSLTL
SDLLAGAAYAANILLSGPLTLKLSPALWFAREGGVFVALT
ASVLSLLAIALERS**LT**MARRGPAPVSSRGRTLMAAAAWG
VSLLLGLLPALGWNCLGRLDACSTVLPLYAKAYVLCVLA
FVGILAAICALYARIYCVVRANARRLPARPGTAGTTSTRA
RRKPRSLALLRTL**SVLLAFVACWG**PLFLLLLLDVACPAR
TCPVLLQADPFLGLAMANSLLNP I IYTL**RDAEMRRTF**RRL
LCCACLRQSTRESVHYTSSAQGGASTRIMLPENGHPLMTP
PFSYLELQRYAASNKSTAPDDLWVLLAQPNQQD

Amend Table 4, beginning on page 35, line 13, by changing the font size and spacing as indicated below (no additions or deletions are to be made to Table 4):

Table 4

PCR Primers for Generating Chimeric Edg 1 Receptors

<u>Primer</u>	<u>Direction</u>	<u>Position</u>	<u>Sequence 5'-3'</u>
Edg-1 (SEQ ID NO:6)		1	CCC/GCG/GTT/AAC/ATG/GGG/CCC/ACC/ AGC/GTC
Edg-3 (SEQ ID NO:7)	rev	1137	CGC/GGA/TCC/TCA/GTT/GCA/GAA/GAT/ CCC
E1/3 CTD (SEQ ID NO:8)		942	CAT/TTA/CAC/TCT/GAC/CAG/CAA/GGA/ GAT/GCG/GCG/G
E1/3 CTD (SEQ ID NO:9)	rev	942	CCG/CAT/CTC/CTT/GCT/GGT/CAG/AGT/ GTA/AAT/GAT/G
E1/3 i2 (SEQ ID NO:10)		402	GTC/TCC/TCG/CCA/TCG/CCA/TCG/AGC/ GGC/ACT/TGA/C
E1/3 i2 (SEQ ID NO:11)	rev	402	GTC/AAG/TGC/CGC/TCG/ATG/GCG/ATG/ GCG/AGG/AGA
E1/3 i2 (SEQ ID NO:12)		441	CGC/CAA/CAA/GAG/GCA/CCG/CCT/CTT/ CCT/GCT/AAT/C
E1/3 i2 (SEQ ID NO:13)	rev	441	GAT/TAG/CAG/GAA/GAG/GCG/GTG/CCT/ CTT/GTT/GGC/G
E1/3 i3 (SEQ ID NO:14)		684	CTA/CTC/CTT/GGT/CAG/GTC/CAG/CAG/ CCG/TAA/GGT/G
E1/3 i3 (SEQ ID NO:15)	rev	684	CAC/CTT/ACG/GCT/GCT/GGA/CCT/GAC/ CAA/GGA/GTA/G
E1/3 i3 (SEQ ID NO:16)		723	CAC/TGC/TGC/GGA/CCG/TGA/TTA/TCG/ TCC/TGA/GCG/TC
E1/3 i3 (SEQ ID NO:17)	rev	723	GAC/GCT/CAG/GAC/GAT/AAT/CAC/GGT/ CCG/CAG/CAG/TG

Amend Table 5, beginning on page 38, line 1, by changing the font size and spacing as indicated below (no additions or deletions are to be made to Table 5):

Table 5

PCR Primers for Generating Chimeric Edg 5 Receptors

<u>Primer</u>	<u>Direction</u>	<u>Position</u>	<u>Sequence 5'-3'</u>
Edg-5 (SEQ ID NO:18)		1	CCC/GCG/GTT/AAC/ATG/GGC/AGC/ TTG/TAC/TCG
Edg-3 (SEQ ID NO:19)	rev	1137	CGC/GGA/TCC/TCA/GTT/GCA/GAA/ GAT/CCC
E5/3 (SEQ ID NO:20)		864	CGT/CAT/CTA/CAC/GTG/GGC/CAG/ CAA/GGA/GAT/GCG/G
E5/3 (SEQ ID NO:21)	rev	864	CCG/CAT/CTC/CTT/GCT/GGC/CCA/ CGT/GTA/GAT/GAC/G
E5/3 i3 (SEQ ID NO:22)		633	CAT/CTA/CTG/CGT/GGT/CAA/GTC/ CAG/CAG/CCG/TAA/G
E5/3 i3 (SEQ ID NO:23)	rev	633	CTT/ACG/GCT/GCT/GGA/CTT/GAC/ CAC/GCA/GTA/GAT/G
E5/3 i3 (SEQ ID NO:24)		723	CAC/TGC/TGC/GGA/CCG/TGA/CCA/ TCG/TGC/TAG/GCG/TC
E1/3 i3 (SEQ ID NO:25)	rev	723	GAC/GCC/TAG/CAC/GAT/GGT/CAC/ GGT/CCG/CAG/CAG/TG

Amend Table 6, beginning on page 39, line 8, by changing the font size and spacing as indicated below (no additions or deletions are to be made to Table 6):

Table 6

PCR Primers for Generating Chimeric Edg 8 Receptors

<u>Primer</u>	<u>Direction</u>	<u>Position</u>	<u>Sequence 5'-3'</u>
Edg-8 (SEQ ID NO:26)		1	CCC/GCG/GTT/AAC/ATG/GAG/TCG/ GGG/CTG/CTG
Edg-4-mut (SEQ ID NO:27)	rev	1149	CGC/GGA/TCC/TCA/GTC/CTG/TTG/ GTT/GGG
E8/4 (SEQ ID NO:28)		920	CCA/TCA/TCT/ACA/CGC/TCC/GAG/ ATG/CTG/AGA/TGC/G
E8/4 (SEQ ID NO:29)	rev	920	CGC/ATC/TCA/GCA/TCT/CGG/AGC/ GTG/TAG/ATG/ATG/G